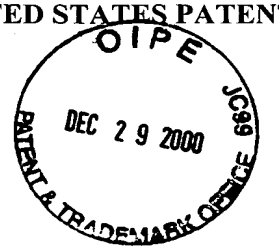
#5 mp 1/4/01

Patent
Attorney's Docket No. 032367-451

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



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In re Patent Application of

Yu-Hua Ji, et al.

Application No.: 09/456,429

Filed: December 8, 1999

For: NOVEL CALCIUM CHANNEL DRUGS AND USES

Group Art Unit: 1614

Examiner: Unassigned

INFORMATION DISCLOSURE STATEMENT TRANSMITTAL LETTER

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Enclosed is an Information Disclosure Statement and accompanying form PTO-1449 for the above-identified patent application.

[X] No additional fee for submission of an IDS is required.

[ ] The fee of $180.00 (126) as set forth in 37 C.F.R. § 1.17(p) is also enclosed.

[ ] A certification under 37 C.F.R. § 1.97(e) is also enclosed.

[ ] A certification under 37 C.F.R. § 1.97(e), and the fee of $180.00 (126) as set forth in 37 C.F.R. § 1.17(p) are also enclosed.

[ ] Charge $_____ to Deposit Account No. 02-4800 for the fee due.

[ ] A check in the amount of $ _____ is enclosed for the fee due.

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Gerald F. Swiss
Registration No. 30,113

P.O. Box 1404
Alexandria, Virginia 22313-1404
(650) 622-2300

Date: December 28, 2000

(11/00)

Patent
Attorney's Docket No. 032367-517

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)
Yu-Hua Ji, et al.) Group Art Unit: 1614
Application No.: 09/456,429) Examiner: Unassigned
Filed: December 8, 1999)
For: NOVEL CALCIUM CHANNEL DRUGS AND USES)

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In accordance with the duty of disclosure as set forth in 37 C.F.R. § 1.56, Applicants hereby submit the following information in conformance with 37 C.F.R. §§ 1.97 and 1.98. Pursuant to 37 C.F.R. § 1.98, a copy of each of the documents cited is enclosed.

1. U.S. Patent No. 3,845,770, issued November 5, 1974, to Theeuwes, et al.
2. U.S. Patent No. 4,326,525, issued April 27, 1982, to Swanson, et al.
3. U.S. Patent No. 4,902,514, issued February 20, 1990, to Barclay, et al.
4. U.S. Patent No. 4,992,445, issued February 12, 1991, to Lawter, et al.
5. U.S. Patent No. 5,001,139, issued March 19, 1991, to Lawter, et al.
6. U.S. Patent No. 5,011,472, issued April 30, 1991, to Aebischer, et al.
7. U.S. Patent No. 5,023,252, issued June 11, 1991, to Hseih.
8. U.S. Patent No. 5,571,827, issued November 5, 1996, to Barberich, et al.
9. U.S. Patent No. 5,616,345, issued April 1, 1997, to Geoghegan, et al.
10. U.S. Patent No. 5,846,839, issued December 8, 1998, to Gallop, et al.
11. U.S. Patent No. 5,891,643, issued April 6, 1999, to Fesik, et al.

12. Canadian Patent No. 2,240,325, published June 11, 1998.

13. International Publication No. WO 93/06121, published April 1, 1993.

14. Alker, D., et al. "Formation, Synthetic Utility and Strucutre Elucidation of a 2-Bromomethyl 1,4-Dihydropyridine." *Tetrahedron Letts.* 31: 1479-1482 (1990)

15. Arrowsmith, et al. "Long-Acting Dihydropyridine Calcium Antagonists. 1. 2-Alkoxymethyl Derivatives Incorporating Basic Substituents." *J. Med Chem.* 29: 1696-1702 (1986).

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18. Bossert, et al. "4-Aruldihydropyridines, a New Class of Highly Active Calcium Antagonists." *Angew. Chem. Int. Ed.* 20: 762-769 (1997).

19. Brittain, et al. "Relaxation of K^+ Contracted Rabbit Aortic Strips Implies Calcium Channel Blockade." *Physiologist*, 28: 325 (1985).

20. Brenner, et al. "Encoded combinatorial chemistry." *Proc. Natl. Acad. Sci., USA*, 89: 5381-5384 (1992).

21. Cremers, et al. "Effects of the Novel T-Type Calcium Channel Antagonist Mibefradil on Human Myocardial Contractility in Comparison with Nifedipine and Verapamil." *J. Cardiovasc. Pharmacol.* 29: 692-696 (1997).

22. Cross, PE., et al. "Selective Class III Antiarrhythmic Agents. 1. Bis(arylalkyl)amines." *J. Med. Chem.* 33(4): 1151-1155 (1989).

23. Eltze, et al. "Stereoselective Inhibition of Thromboxane-Induced Coronary Vasoconstriction by 1,4-Dihydropyridine Calcium Channel Antagonists." *Chirality*, 2: 233-240 (1990).

24. Hess, et al. "Different modes of Ca channel gating behaviour favoured by dihydropyridine Ca agonists and antagonists." *Nature* 311: 538-544 (1984).

25. Hockerman, et al. "Molecular Determinants of Drug Binding and Action on L-Type Calcium Channels." *Annu. Rev. Pharmacol. Toxicol.* 37: 361-96 (1997).

26. Joslyn, et al. "Dimeric 1,4-Dihydropyridines as Calcium Channel Antagonists." *J. Med. Chem.* 31: 1489-1492 (1988).

27. Kokubun, et al., "Studies on Ca Channels in Intact Cardiac Cells: Voltage-Dependent Effects and Cooperative Interactions of Dihydropyridine Enantiomers.." *Molec. Pharmacol.* 30: 571-584 (1986).

28. Liang, R., et al. "Parallel synthesis and screening of a solid phase carbohydrate library." *Science*, 274: 1520-1522 (1996).

29. Osterrieder, W., et al. "In Vitro Phamacologic Profile of Ro 40-5967, a Novel Ca^{2+} Channel Blocker with Potent Vasodilator but Weak Inotropic Action." *Cardiovasc. Pharmacol.* 13: 754-9 (1989).

30. PD-029361. Current drug report.

31. Rampe, D., et al., "New synthetic ligands for L-type voltage-gated calcium channels." *Prog. Drug. Res.* 40: 191-238 (1993).

32. Rovnyak, G.C., et al. "Dihydropyrimidine Calcium Channel Blockers. 4. Basic 3-Substituted-4-aryl-1,4-dihydropyrimidine-5-carboxylic Acid Ester. Potent Antihypertensive Agents." *J. Med. Chem.* 35: 3254-3263 (1992).

33. Tokuma, Y., et al. "Stereoselective pharmacokinetics of dihydropyridine calcium antagonists." *J. Chromatography A.*, 694: 181-193 (1995).

34. Yuen, P., et al. "Synthesis and SAR of sibustituted 1,2,3,4-tetrahydroisoquinoloines as N type Calcium channel blockers." *Bioorg and Med. Chem. Lett.* 8: 2415 (1998).

Additionally, the following documents were cited in the International Search Report for the related PCT Application No. PCT/US99/12672. A copy of the International Search Report is enclosed for the convenience of the Examiner.

35. U.S. Patent No. 4,771,057, issued September 13, 1988, to Knaus, et al.

36. International Publication No. WO 92/05802, published April 16, 1992.

37. International Publication No. WO 97/21445, published June 19, 1997.

38. International Publication No. WO 98/00439, published January 8, 1998.

39. International Publication No. WO 98/34948, August 13, 1998.

40. Denyer, et al. "HTS Approaches to Voltage-Gated Ion Channel Drug Discovery ." Drug Discovery Today. 3(7): 323-332 (1998).

41. Gordeev, et al. "A General and Efficient Solid Phase Synthesis of Qyinazoline-2,4-

diones." Tetrahedron Lett. 38(10): 1729-1732 (1997).

42. Gordeev, et al. "Approaches to Combinatorial Synthesis of Heterocycles: A Solid Phase Synthesis of 1,4-Dihydropyridines." J. Org. Chem. 61: 924-928 (1996).

43. Kenny, et al. "The Application of High-throughput Screening to Novel Lead Discovery." Progress in Drug Research. Edited by Ernst Jucker. Herhauser Verlag: Basel, 1998, Vol. 1, 246-269.

44. Shuker, S.B., "Discovering High-Affinity Ligands for Proteins, SAR by NMR." Science. 274: 1531-1534 (1996).

The following documents were cited in the Written Opinion for the related PCT Application No. PCT/US99/12672.

45. U.S. Patent No. 5,463,564 A, issued October 31, 1995, to Agrafiotis, et al.

46. U.S. Patent No. 5,686,495, issued November 11, 1997, to Goldwin, et al.

47. Portoghese, P.S. "The Role of Concepts in Structure-Activity Relationship Studies of Opioid Ligands." *J. Med. Chem.* 35(11): 1927-1937 (1992).

48. Zeng, et al. "Automated Analytical/Preparative High Performance Liquid Chromatography-Mass Spectrometry System for the Rapid Characterization and Purification of Compound Libraries." *J. Chrom. A.* 794:3-13 (1998).

The Examiner's attention is directed to copending applications number 09/493,081, filed January 28, 2000, for Griffin, et al. (copy not enclosed), and 09/674,422, filed November 1, 2000, for Ji, et al. (copy not enclosed), and the documents cited therein.

☐ **In accordance with MPEP § 609(c)(2) (July 1998, page 600-112), the Office is requested to return a copy of this Information Disclosure Statement with the Examiner's initials adjacent to this paragraph indicating that these copending applications have been considered. By citation to the copending applications, confidentiality is not waived and the Office is requested to maintain the confidentiality of the copending applications under 35 U.S.C. § 122.**

This IDS is being filed prior to a first Office Action on the merits, therefore no fee or certification is required under 37 C.F.R. § 1.97(b). In the event that an Office Action is mailed prior to receipt of this paper, the Commissioner is hereby authorized to charge the requisite fees under 37 C.F.R. § 1.97(c) for submission of this paper to Deposit Account No. 02-4800.

To assist the Examiner, the documents are listed on the attached form PTO-1449. It is respectfully requested that an Examiner initialed copy of this form be returned to the undersigned.

Respectfully submitted,
BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Gerald F. Swiss
Registration No. 30,113

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